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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,840	12/31/2001	Xiang-Jin Meng	AM100389	5348

7590 11/17/2004

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,840	MENG ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6,8-15,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *3,6,8-15,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The examiner of your application has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1648, Examiner Foley.

It is noticed in the firth paragraph of the previous Office action and in the first paragraph of the instant response, a typographical error was made with respect to claims 19 and 20. These claims were not withdrawn from consideration and these claims are also not cancelled. In the amendment received June 30, 2004, applicant cancelled claims 4, 5, 7, 17 and 18. Claims 1, 3, 6, 8-15, 19 and 20 are pending and under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant states that the claims have been amended to overcome all of the previous rejections. However, the amendments do not remedy all of the rejections of record.

Claim 3 remains unclear because it cannot be determined what is intended by "a polynucleotide" since this still may refer to a single nucleotide. Claim 3 also remains indefinite because it is not clear whether the complementary polynucleotide must hybridize over the entire length of SEQ ID NO: 1, or if hybridization over some portion of its length is sufficient to meet the requirements of the claims. It is noted that claim 8

(d) also recites this same ambiguous language. This rejection also affects al dependent claims.

Claim 6 remains indefinite because it is not understood how an isolated virus can have an "isolated" polynucleotide. Second, the Markush group recited in claim 6 is redundant since claim 3 recites the same "nucleotide sequence set forth in SEQ ID NO:1 or its complementary strand" as specifically recited again in claim 6. This rejection also affects al dependent claims.

Claim 8 remains indefinite because it cannot be determined how SEQ ID NO: 1 or its complementary strand can be a common characteristic of all of a modified live, an inactivated, and an attenuated virus. This rejection also affects al dependent claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising an isolated avian hepatitis E virus having the nucleotide sequence as set forth in SEQ ID NO: 1, does not reasonably provide enablement for a vaccine comprising an isolated avian hepatitis E virus that confers protection against a viral infection or disease, or for a method of vaccination using such a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is maintained for reasons of record.

Applicant points to the working examples demonstrating that avian HEV is antigenically related to Sar-55 HEV and swine HEV. Applicant asserts that the evidence presented regarding cross-reactivity proves that there is a reasonable likelihood that antibodies will be produced from challenge by HEV vaccination. Applicant also cites the teachings of Schofield et al., which shows the generation of neutralizing Mabs against the capsid protein of human HEV. Applicant states that the neutralizing epitope is also located within the avian HEV that reacted with human and swine HEV anti-sera. Applicant discusses the Jennerian approach in FIELDS VIROLOGY that was used to develop various attenuated viruses. Applicant concludes that the strong antigenicity of the instant avian HEV and conventional techniques in the art for developing attenuated viruses enables the skilled artisan to formulate a vaccine.

Applicant's arguments and a review of Schofield et al. have been fully considered, but are found unpersuasive. The instant claims are drawn to a vaccine against avian and mammalian HEV comprising a modified live avian HEV, an inactivated avian HEV or an attenuated HEV. All of these ingredients comprise the nucleotide sequence as set forth in SEQ ID NO: 1 or its complementary strand. In addition, the vaccine may also comprise a polynucleotide that hybridizes to the nucleotide sequence as set forth in SEQ ID NO: 1.

With respect to the antigenic relationship of the instant avian HEV to other HEV's, neither the specification or the prior art demonstrate that vaccination with avian HEV is protective against all avian HEV in fowl. It remains unclear how the skilled artisan would be able to immunize a host-specific HEV with an avian HEV. Although the Jennerian approach is well utilized in the virus art and has produced some attenuated

viruses, it is noted that this approach has not worked with all hepatitis viruses. Therefore, it remains unpredictable as to whether this approach will be successful for the instant avian HEV to produce a vaccine against any HEV infection. Due to some evidence of cross-relatedness with the instant avian HEV and other HEVs, applicant has concluded that neutralizing antibodies would be generated upon administration of the instant avian HEV. Applicant has pointed to the teachings of Schofield et al. as further evidence. However, the HEV administered by Schofield et al. is already neutralized in vitro with the incubation with certain Mabs, see the abstract, the paragraph bridging pages 5549-5550 and the second paragraph on page 5553. Schofield et al. propose administering the neutralizing antibodies against HEV infection, not the virus itself, see the last two paragraphs of 5553. Schofield et al. also do not propose or suggest cross-vaccinating various hosts against HEV, even though the neutralizing epitope is found in humans and swine, see the paragraph bridging the columns on page 5548. Therefore, it is maintained that the instant claims would require undue experimentation by one skilled in the art to make and use the instant vaccine claimed.

Claim 8 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant states that the claim has been amended to obviate the rejection. However, the claim still recites language that is unsupported by the disclosure, "A vaccine...selected from the group consisting of: (d) a polynucleotide which hybridizes to

the nucleotide sequence as set forth in SEQ ID NO: 1." Applicant is required to either point to where support for this language can be found or cancel the new matter.

Claims 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of propagating an HEV having a nucleotide sequence as set forth in EQ ID NO: 1 in an embryonated chicken egg, does not reasonably provide enablement for attenuating the virus by serially passaging the virus until the virus is rendered attenuated. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Applicant rejects the failing of Theiler as irrelevant to the instant case. Applicant discusses the Jennerian approach that has been used to develop various vaccines and concludes that the skilled artisan does not need to know the mechanism of attenuation. Applicant asserts that predictability does not require actual reduction to practice, but only whether an ordinary virologist would have a reasonable doubt as to whether HEV can be attenuated through conventional serial passage in eggs. Applicant states that guidance provided in the specification as well as common knowledge in the art provides sufficient teaching for the skilled artisan to be able to practice the methods claimed without undue effort.

Applicant's arguments have been fully considered, but are found unpersuasive. Contrary to applicant's assertion, the teachings of Theiler are relevant to whether an ordinary virologist would be able to predict whether the instant method would result in an effectively attenuated virus. The instant disclosure does not provide a working example demonstrating sufficient attenuation with the instant virus. Therefore, actual reduction to

practice in the vaccine art is required for review. In the authoritative reference of FIELDS VIROLOGY, it is evident that making attenuated viruses is unpredictable for several reasons, such as an experimental system for evaluating attenuations for HEV. Although propagation of viruses and attenuation of some viruses is known in the art, there is no guidance provided by the disclosure or the prior art for whether the avian HEV claimed would evolve sufficient mutations for attenuation while retaining a balance of immunogenicity to induce the required protective immune response in avians and any other HEV susceptible host. For example, the ordinary virologist would be unable to predict whether the cross-reactive epitope discussed previously would be abolished or not during serial passaging. For these reasons, the rejection is maintained for reasons of record.

Allowable Subject Matter

Claim 1 is allowed. As states previously, claim 3 would also be allowable if the previous suggestion is implemented.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the

advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 10:00 AM - 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Primary Examiner
Art Unit 1648